Race-Related Differences in HLA Association with Ankylosing Spondylitis and Reiter's Disease in American Blacks and Whites

Muhammad A. Khan, MD, MRCP
Cleveland, Ohio

Ankylosing spondylitis is three times less common in American blacks than in whites. It is extremely rare in African blacks of unmixed ancestry. A histocompatibility antigen HLA-B27, which does not exist in African blacks of unmixed ancestry, and is present in eight percent of white and two to four percent of the American black population, is strongly associated with ankylosing spondylitis and Reiter's disease. B27 is present in more than 80 percent of white patients with ankylosing spondylitis or Reiter's disease but in less than 60 percent of American black patients. Other genetic and environmental factors may be of major importance in the genesis of these diseases in American blacks. For diagnostic purposes the absence of B27 is of less importance in excluding these diseases in blacks than in whites.

A variety of human diseases have recently been found to occur more frequently in individuals possessing certain antigens called histocompatibility or tissue antigens.[1] These antigens are genetically determined glycoproteins present on cell membranes. They are also known as human leukocyte antigens (HLA) because they were originally discovered on leukocytes. The outstanding example of an association between an HLA antigen and a disease is the one between HLA-B27 (or simply B27) and ankylosing spondylitis (AS).[2,3]

There is appreciable variation in the frequency of B27 in different races[4,5] and the prevalence of AS tends to parallel the B27 frequency in the population.[5,6] B27 is absent in African blacks of unmixed ancestry,[4] and AS is extremely rare in this population; only a few isolated cases have been reported.[7-10] B27 is present in eight percent of the American white population.[3,4,11] Approximately 1.8 percent of American whites suffer from AS,[5] a relatively high disease prevalence. Two to four percent of American blacks possess B27,[4,5,11] presumably a result of racial admixture with whites over the past two centuries. There is indirect evidence indicating that the prevalence of AS in American blacks is one third of that in whites.[12]

We have studied a large number of patients, both black and white, suffering from AS and related diseases.[11,13,14] The purpose of the present article is to review briefly the subject of HLA association with AS and Reiter's disease (RD) in American blacks, to note the differences from whites, and also to emphasize the clinical relevance and importance of these findings.

In 1973, it was first noted that B27 is present in 80 to 95 percent of white patients with AS or RD[2,3,15,16] while being present in only eight percent of the normal controls. Detection of this antigen has been reported to serve as a valuable diagnostic aid in these diseases in both whites and blacks.[17,18] Bluestone has stated that, in the absence of the bacteriological proof of gonococcal infection, the absence of B27 almost rules out the possibility of Reiter's disease both in whites and blacks.[17] As we shall see, not all of these statements have been borne out by subsequent studies.

The frequency of B27 among American blacks with AS has, in fact, been found to be only about 50 to 60 percent rather than the 90 to 95 percent seen in white patients.[11,13,18-20] This suggests that for diagnostic purposes the absence of B27 is of less importance in excluding AS in black patients than in whites, since one would expect approximately 40 to 50 percent false-negative results in the former and only five to ten percent in the latter.[11,13,20] An American white who possesses B27 has 150 to 180 times greater risk of developing AS as compared to the one who lacks it.[1,11] The comparable figure for a B27-positive American black is 54.[11] We have recently noted a subgroup among the B27-negative black patients with AS whose disease seems to be associated with HLA-B7.[21] These B7-positive patients tend to lack familial

Dr. Khan is Assistant Professor of Medicine, Case Western Reserve University at Metropolitan General Hospital, Cleveland, Ohio. Requests for reprints should be addressed to Dr. Muhammad A. Khan, 3395 Scranton Road, Cleveland, Ohio 44109.

aggregation of AS and are older at onset of their disease than the B27-positive patients.[22]

RD has not been well studied in blacks, and no clear data are available regarding the prevalence of this disease in either African or American blacks. From the few reports that have been published, it is clear that the majority of black patients with RD do not possess B27.[13,19] Testing for B27 is thus much less useful in diagnosing RD in blacks than in whites.

In conclusion, AS is less common in American blacks than in whites. Susceptibility to AS or RD is not as closely associated with B27 in blacks as in whites. Other genetic and environmental factors may be of major importance in the genesis of these diseases, particularly in American blacks. For diagnostic purposes, the absence of B27 is of less importance in excluding AS or RD in black patients than in whites.

Literature Cited

1. McDevitt HO, Bodmer WF: HL-A, immune-response genes, and disease. Lancet 1:1269-1275, 1974
2. Brewerton DA, Caffrey M, Hart FD, et al: Ankylosing spondylitis and HL-A 27. Lancet 1:904-907, 1973
3. Schlosstein L, Terasaki PI, Bluestone R, et al: High association of an HL-A antigen, W27, with ankylosing spondylitis. N Engl J Med 288:704-706, 1973
4. Payne R, Feldman M, Cann H, et al: A comparison of HLA data of the North American black with African black and North American Caucasoid populations. Tissue Antigens 9:135-147, 1977
5. Woodrow JC: Histocompatibility antigens and rheumatic diseases. Semin Arthritis Rheum 6:257-276, 1977
6. Omenn GS: Significance of histocompatibility genes in rheumatology. Arthritis Rheum 20:484-496, 1977
7. Mulley GP: Ankylosing spondylitis in blacks. Lancet 1:1209, 1977
8. Klemp P, Meyers OL: Ankylosing spondylitis in a Xhosa father and daughter. S Afr Med J 50:1439-1441, 1976
9. Solomon L, Beighton P, Valkenburg HA, et al: Rheumatic disorders in the South African Negro. S Afr Med J 49:1292-1296, 1975
10. Davies AGM, Vaizey JM: Spondylitis ankylopoietica in a Uganda African. Br Med J 1:106, 1961
11. Khan MA, Braun WE, Kushner I, et al: HLA B27 in ankylosing spondylitis: Differences in frequency and relative risk in American blacks and Caucasians. J Rheumatol 4 (suppl 3):39-43, 1977
12. Baum J, Ziff M: The rarity of ankylosing spondylitis in the black race. Arthritis Rheum 14:12-18, 1971
13. Khan MA, Kushner I, Braun WE: Low incidence of HLA-B27 in American blacks with spondyloarthropathies. Lancet 1:483, 1976
14. Khan MA, Kushner I, Braun WE: Comparison of clinical features in HLA-B27 positive and negative patients with ankylosing spondylitis. Arthritis Rheum 20:909-912, 1977
15. Brewerton DA, Nicholls A, Oates JK, et al: Reiter's disease and HLA-27. Lancet 2:996-998, 1973
16. Morris R, Metzger AL, Bluestone R, et al: HL-A W27—a clue to the diagnosis and pathogenesis of Reiter's syndrome. N Engl J Med 290:554-556, 1974
17. Bluestone R: HL-A antigens in clinical medicine. DM 23(1):1-27, 1976
18. Kemple K, Bluestone R: The histocompatibility complex and rheumatic diseases. Med Clin North Am 61:331-345, 1977
19. Good AE, Kawanishi H, Schultz JS: HLA B27 in Blacks with ankylosing spondylitis or Reiter's disease. N Engl J Med 294:166-167, 1976
20. Ruderman RJ, Ward FE: HLA-B27 in black patients with ankylosing spondylitis. Lancet 1:610, 1977
21. Khan MA, Kushner I, Braun WE, et al: HLA-B7 and ankylosing spondylitis in American blacks. N Engl J Med 297:513, 1977
22. Khan MA, Kushner I, Braun WE: Association of HLA-B7 with ankylosing spondylitis in HLA-B27 negative American black patients. Clin Res 25:582A, 1977

New Philippine and West African Gonorrhea Strains Destroy Penicillin

Two new strains of gonorrhea that completely destroy penicillin have appeared in the Philippines and West Africa. So far, only about 150 cases of the Philippine strain have been reported in 22 states in the United States and in 15 foreign countries. Although no cases of the West African strain, which is genetically different from the Philippine strain, have appeared in the United States, it has been seen in Great Britain. Both strains carry genes for production of a penicillin-destroying enzyme.

If the penicillin-destroying strain becomes widespread, which is possible, the next available antibiotic against gonorrhea is spectinomycin. However, some strains of gonococci have been found also to develop resistance to spectinomycin and it costs six times as much as penicillin.

International Symposium on Psoriasis Therapy

Dr. Eugene M. Farber of Stanford and Dr. Felix Sagher of Jerusalem will co-chair a symposium on psoriasis therapy sponsored jointly by the Departments of Dermatology of Stanford University School of Medicine and Hadassah University Hospital in Israel, February 19-26, 1978. An international faculty will participate.

Drew Plaque Unveiled in New Dunbar High School

A plaque honoring Dr. Charles R. Drew was unveiled on September 23, 1977, in the office corridor of the new Dunbar High School building. The plaque was donated by the family of the late Robert N. Mattingly, long-time principal of Cardozo High School in Washington and historian of the M Street and Dunbar High Schools.